UNITED STATES DISTRICT COURT
NORTHERN DISTRICT OF ILLINOIS

IN RE: TESTOSTERONE REPLACEMENT THERAPY PRODUCTS LIABILITY LITIGATION	MDL No. 2545
THIS DOCUMENT RELATES TO: *Tracy Garner v. Eli Lilly and Company; Lilly USA, Inc.* Case No. 1:15-cv-2045 *John Debroka Jr. v. Eli Lilly and Company; Lilly USA, LLC* Case No. 1:15-cv-9246	Master Docket Case No. 1:14-cv-01748 Honorable Matthew F. Kennelly

DEFENDANTS ELI LILLY AND COMPANY AND LILLY USA, LLC'S MOTION AND MEMORANDUM OF LAW IN SUPPORT OF
MOTION TO EXCLUDE EXPERT TESTIMONY

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Defendants Eli Lilly and Company and Lilly USA, LLC (erroneously sued and served as Lilly USA, Inc.) (collectively, "Lilly") hereby move to exclude all of plaintiffs' expert testimony pursuant to Fed. R. Evid. 702. Lilly's Memorandum of Law follows, and supporting Declarations and Exhibits are filed herewith.

I. INTRODUCTION

The unique facts in these two cases present fundamentally different issues than the prior *Daubert* motions considered by this Court to date. Plaintiff Garner alleges that the use of Axiron® for only four days caused his heart attack. And Plaintiff Debroka alleges DVT despite his irregular and minimal use of Axiron®, that had stopped well before his clot developed. Plaintiffs rely on the same experts offered before – causation experts Hossein Ardehali and Henry Rinder, regulatory expert Peggy Pence, biostatistician Martin Wells, epidemiologist Burt Gerstman, and marketing expert David Handelsman – but none of them has adapted his or her opinions to these cases and the bases and rationale of their earlier opinions do not fit the facts of either Plaintiff's case.

For instance, the off-the-shelf opinions of Garner's causation expert, Dr. Ardehali, and his epidemiology expert, Dr. Gerstman, do not fit the extremely short duration of Garner's use of Axiron®. His biostatistics expert, Dr. Wells, offers an opinion that does not satisfy Garner's burden of proof under Alabama law. Likewise, Debroka's causation expert, Dr. Rinder, offers opinions that do not fit the facts peculiar to Debroka's Axiron® use. Debroka has also notified Lilly that he will offer the opinions of one of his treating physicians, Dr. Tache; but Dr. Tache's opinions exceed the bounds of permissible opinions for a non-retained expert who has not submitted an expert report under Fed. R. Civ. P. 26(a)(2)(B).

In addition, Plaintiffs' remaining experts have little basis for offering Axiron®-specific opinions. Dr. Pence, for example, lacks any information specific to Axiron®. And Dr.

Handelsman recycles opinions he has asserted against other manufacturers, but does not tie his analysis to anything relevant to Lilly's marketing of Axiron®. Indeed, he candidly admits that he did not even review any of Lilly's materials and readily acknowledged that he has no basis to tie any of his theories to these Plaintiffs or their prescribers.

Lilly's motion to exclude Plaintiffs' experts accordingly should be granted for reasons unique to these bellwether cases.

II. LEGAL STANDARD

Rule 702 of the Federal Rules of Evidence governs the framework for the admissibility of expert testimony. It provides:

> A witness who is qualified as an expert by knowledge, skill, experience, training, or education may testify in the form of an opinion or otherwise if:
>
> (a) the expert's scientific, technical, or other specialized knowledge will help the trier of fact to understand the evidence or to determine a fact in issue;
>
> (b) the testimony is based on sufficient facts or data;
>
> (c) the testimony is the product of reliable principles and methods; and
>
> (d) the expert has reliably applied the principles and methods to the facts of the case.

Fed. R. Evid. 702. "[C]lose judicial analysis of expert testimony is necessary 'because expert witnesses are not necessarily unbiased scientists.'" *Nelson v. Tenn. Gas Pipeline Co.*, 243 F.3d 244, 252 (6th Cir. 2001) (quoting *Turpin v. Merrell Dow Pharm., Inc.*, 959 F.2d 1349, 1352 (6th Cir. 1992)). Thus, the court "plays the role of gatekeeper in determining whether proposed expert testimony meets the standards of Rule 702." *In re Testosterone Replacement Therapy Prods. Liab. Litig.*, No. 14 C 1748, 2017 WL 1833173, at *5 (N.D. Ill. May 8, 2017) ("CMO 46"). In that role, it must determine "(1) whether the witness is qualified, (2) whether the

expert's applied methodology is scientifically reliable, and (3) whether the testimony will assist the trier of fact to understand the evidence or determine a fact in issue." *Id.* (citing *Myers v. Ill. Cent. R.R. Co.*, 629 F.3d 639, 644 (7th Cir. 2010)). Moreover, Plaintiffs bear the burden to establish by a preponderance of the evidence that their experts' proposed testimony satisfies these requirements. *See* CMO 46, at *6.

In looking at the experts' qualifications, the issue is not whether an expert is qualified in general. Rather, the expert's qualifications must provide a foundation for her to answer the specific question posed in the particular case. *Id.* at *5.

With respect to reliability, the focus "must be solely on principles and methodology, not on the conclusions that they generate." *Id.* (citing *Daubert v. Merrell Dow Pharms., Inc.*, 509 U.S. 579, 595 (1993)). The expert must provide some "reliable basis" for the conclusions that he reaches. *See id.* "[A]n expert must explain the methodologies and principles that support his or her opinion" (*In re Yasmin and YAZ (Drospirenone) Mktg., Sales Pracs. and Prods. Liab. Litig*, No. 3:09-md-02100-DRH-PMF, 2011 WL 6302287, at *3 (S.D. Ill. Dec. 16, 2011)), and then the trial judge must "evaluate the data offered to support an expert's bottom-line opinions to determine if that data provides adequate support to mark the expert's testimony reliable" (*Brown v. Nucor Corp.*, 785 F.3d 895, 936 (4th Cir. 2015)). If there is "too great an analytical gap between the data and the opinion proffered[,]" the court should exclude the testimony. *Gen. Elec. Co. v. Joiner*, 522 U.S. 136, 146 (1997).

Finally, in order to assist the trier of fact, the proffered expert opinion must "fit" the facts of the case and have "a valid scientific connection to the pertinent inquiry." CMO 46, at *5 (citing *Daubert*, 509 U.S. at 591-92). A district court should exclude "opinion evidence that is connected to existing data only by the *ipse dixit* of the expert." *Joiner*, 522 U.S. at 146.

III. ARGUMENT

A. No Admissible Expert Testimony Supports Garner's Cardiovascular Claims

Unlike previous CV bellwether plaintiffs, Garner claims that Axiron® caused his March 13, 2013 heart attack after he used the product for only four days. As a result, his general and specific causation expert, Dr. Hossein Ardehali, and his epidemiology expert, Dr. Burt Gerstman, fail to offer opinions that fit Garner's unique facts. And Garner's biostatistician, Dr. Martin Wells, offers a general causation opinion that similarly fails to satisfy Garner's burden of proof under Alabama law. All of these experts' opinions should be excluded.

1. Dr. Ardehali's Opinions Should Be Excluded

a. Dr. Ardehali's Litigation-Driven Specific Causation Opinion Does Not Satisfy *Daubert*'s Standards of Admissibility

As he has done consistently in earlier cases, Dr. Ardehali has opined that TRT caused a plaintiff's cardiovascular event. He reaches his specific causation conclusion even though he cannot point to a single study – or to even one patient in any study – where four days of TRT use was found to cause a cardiovascular event. (Ardehali Dep., Ex. 1 to Declaration of Mildred Y. Segura in support of Motion to Exclude Expert Testimony ("Segura Decl."), at 109:17-112:8). This omission alone renders his opinion inadmissible. *See In re Accutane Prods. Liab.*, 511 F. Supp. 2d 1288, 1292-94, 1302-03 (M.D. Fla. 2007), *aff'd*, 378 F. App'x 929 (11th Cir. 2010) (excluding plaintiffs' causation expert who ignored the dose-response relationship and opined that Accutane caused the alleged injuries "no matter what the dose, no matter how long it ha[d] been since the individual last took Accutane, and, seemingly, no matter what other background factors [were] present"); *see also, e.g.*, *In re Bextra & Celextra Mktg. Sales Pracs. & Prod. Liab. Litig.*, 524 F. Supp. 2d 1166, 1175-81 (N.D. Cal. 2007) (excluding testimony where no studies supported the alleged dose-response relationship). Apart from that, Dr. Ardehali also reaches his

conclusion without meaningful consideration of Garner's risk factors, and while simultaneously acknowledging that it would not have been "unusual" if Garner had had a heart attack in the absence of TRT use. (*See* Ardehali Dep. at 136:1-137:23 ("everybody is at risk" for a heart attack after the age of 40)). Faced with such negligible usage and an extensive range of longstanding risk factors, Dr. Ardehali must do more than simply regurgitate his standard "always TRT" conclusion.

An expert must "'employ[] in the courtroom the same level of intellectual rigor that characterizes the practice of an expert in the relevant field.'" *In re Testosterone Replacement Therapy Prods. Liab. Litig.*, Case No. 14 C 1748, 2017 WL 4772759, at *6 (N.D. Ill. Oct. 23, 2017) ("CMO 76") (quoting *Kumho Tire Co. v. Carmichael*, 526 U.S. 137, 152 (1999)). When an expert's opinions are driven by what is needed in litigation, there is reason to question the reliability of those opinions. *See, e.g.*, *In re Mirena IUD Prod. Liab. Litig.*, 169 F. Supp. 3d 396, 440 (S.D.N.Y. 2016). In this case, Dr. Ardehali's litigation-driven specific causation opinion – the same opinion he always offers, notwithstanding the facts and the contrary evidence specific to Garner – lacks the requisite "intellectual rigor," and should be excluded.

b. Dr. Ardehali Fails to Reliably Apply His Differential Etiology

Tipping his hand about his foregone conclusion, Dr. Ardehali has this to say about his starting assumption:

> Q. So any patient who walks in your office and tells you they had a heart attack and they used a testosterone product beforehand, you are pretty much going to conclude that the heart attack was caused by the testosterone?
>
> A. I'm going to tell them that was a major contributing factor and it has happened before, and I tell them do not take this product ever again.

*(*Ardehali Dep. at 159:9-16). Nevertheless, Dr. Ardehali purports to employ a differential etiology in arriving at his conclusion that Axiron® caused Garner's heart attack. But to be

reliable, Dr. Ardehali "'must do more than just state that []he is applying a respected methodology, []he must follow through with it.'" CMO 46, at *17 (quoting *Brown v. Burlington N. Santa Fe Ry. Co.*, 765 F.3d 765, 773 (7th Cir. 2014)).

First, a proper differential etiology requires that an expert reliably rule in all "reasonable" potential causes. *In re Zimmer Nexgen Knee Implant Prod. Liab. Litig.*, 218 F. Supp. 3d 700, 716 (N.D. Ill. 2016) (citation omitted). Next, the expert must "meaningfully consider" other risk factors that could have been responsible for plaintiff's injury. *Brown*, 765 F.3d at 773-74 (quoting *Schultz v. Akzo Novel Paints, LLC*, 721 F.3d 426, 433 (7th Cir. 2013)). "[A] differential diagnosis that fails to take serious account of other potential causes may be so lacking that it cannot provide a reliable basis for an opinion on causation." *Guinn v. AstraZeneca Pharms. LP*, 602 F.3d 1245, 1253 (11th Cir. 2010); *see also* CMO 46, at *17 (an expert must explain why he does not think the alternative explanations were the sole cause of plaintiff's injury); *In re Trasylol Prods. Liab. Litig.*, No. 08-MD-01928, 2011 WL 7109295, at *7 (S.D. Fla. Feb. 4, 2011) (an expert who fails to "rigorously consider and rule out other potential sole causes" of plaintiff's alleged injury has not appropriately applied the differential etiology method).[1]

Here, rather than "reliably ruling in" Axiron® and giving "meaningful consideration" to alternative explanations, Dr. Ardehali simply assumes that any time a patient suffers a heart attack while using Axiron®, Axiron® must have played a role in causing the patient's heart attack. Indeed, Dr. Ardehali went so far as to testify that if a patient had used Axiron® for just

[1] *Accord In re Trasylol Prods Liab. Litig.*, No. 08-MD-1928, 2013 WL 3353833, at *10-*12 (S.D. Fla. July 3, 2013) (excluding expert's differential etiology as unreliable where he failed to account for or appropriately address – by giving them "short shrift" at the rule-out phase, or dismissing them without discussion – numerous risk factors that, alone or in combination, could have contributed to plaintiff's alleged injury); *In re Lipitor (Atorvastatin Calcium) Mktg., Sales Pracs. & Prods. Liab. Litig.*, 185 F. Supp. 3d 786, 805 (D.S.C. 2016) (finding expert's differential diagnosis unreliable where he "fail[ed] to consider several risk factors at all").

one day, he would say Axiron® was a "major contributing factor" to a resulting heart attack; this opinion is admittedly devoid of support in the relevant literature or clinical experience, and is unaffected by the fact that Garner had been using Axiron® for only four days. (Ardehali Dep. at 153:2-154:21). Nor would Dr. Ardehali's opinion have changed if Garner had been taking Axiron® for five years (*id.* at 155:2-12), or if Garner had stopped taking Axiron® six months before his heart attack. (*Id.* at 155:17-156:11). On the contrary, for virtually every hypothetical that could be posed, he admitted that if a patient were using Axiron® at the time of a heart attack, he would conclude that Axiron® was the cause:

> Q. Hypothetically, again, other than the fact that he used Axiron, what medical facts would need to change about his history before you would reconsider your opinion about whether Axiron caused his heart attack?
>
> A. Well, I guess there wouldn't be anything unless he was, let's say, 15 years old and he was taking testosterone for a disease.

(*Id.* at 158:21-159:4). Leaving no doubt about his unflinching belief, Dr. Ardehali says this about his "always TRT" opinion: "If you are a patient who is at high risk and you take testosterone replacement therapy, that by itself is sufficient for me to conclude that was a major contributing factor." (*Id.* at 159:5-8).

Given Dr. Ardehali's unyielding causation assumption, it is not surprising that he failed to "meaningfully consider" several of Garner's pre-existing risk factors before summarily dismissing them as alternative causes of his heart attack. Dr. Ardehali failed to consider Garner's prior stroke in 2007 or his diagnosed hypertension and dyslipidemia (Ardehali Dep. at 72:1-73:4), and he did not take into account family history of heart disease, despite the fact that Garner himself testified that his father died of a heart attack (*id.* at 74:18-76:12). The only pre-existing risk factor Dr. Ardehali would concede was smoking, and even then he significantly underestimated Garner's pack-year history. (*See id.* at 71:17-24, 100:8-104:22 (applying a 13.5

pack-year history instead of a 27 to 40 pack-year history)). Plainly, Dr. Ardehali never "meaningfully considered" these alternative causes of Garner's heart attack – indeed, he testified that he did not "rule in" any of these conditions as risk factors for Garner – and nowhere did he explain why these alternative causes could not have been the sole cause of the heart attack.

As this record shows, Dr. Ardehali's specific causation opinion aligns with opinion testimony this Court excluded in the AbbVie bellwether cases when offered by Dr. Setaro. There, the Court found that Dr. Setaro did "not point to anything about [the plaintiff's] case in particular to suggest his injury was the result of [testosterone] rather than the multiple other risk factors that Dr. Setaro was unable to rule out." CMO 46, at *22. Similarly here, Dr. Ardehali does not explain why Axiron®, and not some combination of Garner's history, his family's history, and his hypertension, dyslipidemia, and smoking, caused Garner's heart attack. Dr. Ardehali did not even acknowledge most of these as risk factors, and never even ruled any of them in as possible alternate causes. (*See* Ardehali Dep. at 72:1-73:4, 74:18-76:12, 77:2-9). By contrast, Dr. Ardehali was permitted to testify in the Holtsclaw case because he did "rule in" all of the plaintiff's other risk factors and, while he believed they contributed to the plaintiff's "chronic inflammatory disease," he ruled out each of them out as the likely "sole cause" of the plaintiff's injury. CMO 76, at *8.

In sum, because Dr. Ardehali failed to reliably "rule in" Axiron, given the fact that Garner used the product for only four days, and he failed to meaningfully consider and rule out possible contributing or alternate causes of Garner's heart attack, his specific causation opinion is not the result of a reliable methodology and should be excluded.

c. Certain of Dr. Ardehali's Specific Causation Opinions Are Inadmissible

Several of Dr. Ardehali's specific causation opinions lack foundation and should be excluded for this reason.

First, Dr. Ardehali opines that "testosterone replacement therapy causes a bigger clot formation that can cause blockage in the coronary vessel, and that's what happened in Garner." (Ardehali Dep. at 142:20-23; *see also id.* at 143:12-18, 144:7-10 ("I think the major factor that played a role was the actual increase in the size of the clot when it was formed.")). When questioned, Dr. Ardehali could not point to any medical literature confirming that TRT causes bigger clots to form, and admitted that he had no actual evidence that TRT made Garner's clot bigger:

> Q. And in terms of making conclusions about the size of the thrombus, how are you able to tell that the size of the thrombus was bigger because he was on testosterone than a patient who may not have been on testosterone? Do you understand my question?
>
> A: I think I do, but all I can tell you is that the size of the thrombus was big enough to cause complete blockage in the coronary vessel. So that's all I can tell you, that there was a thrombus that was large enough to cause total blockage.

(*Id.* at 158:9-20).

Second, although Dr. Ardehali posits that Garner had some unidentified "chronic inflammatory disease" that reacted with Axiron® and caused his heart attack, he admits that he has no evidence to support this theory. (*See* Ardehali Garner Report, Ex. 2 to Segura Decl., at p. 10). During his deposition, Dr. Ardehali explained that some patients have "this chronic inflammatory process going on in them," and that there are markers of this process, called CRP; such patients are at a high risk of CV events. (Ardehali Dep. at 78:7-18). Yet he conceded that this CRP measurement was never done for Garner:

> Q. Is there any testing that's been done in Mr. Garner which suggests that he had a chronic inflammatory process?
>
> A. In this specific case there was no CRP checked, that's correct.
>
> Q. So beyond aging, is there any evidence of a chronic disease that Mr. Garner had that would explain his low testosterone?
>
> A. Well, again, you know, he has – he is a smoker, you know, and smoking again is associated with some, you know, increase in inflammatory process, and other than that, no.
>
> Q. Is there any literature out there which links smoking with a chronic inflammatory process that can lower testosterone levels?
>
> A. That can lower testosterone?
>
> Q. Yeah.
>
> A. No, but smoking has been shown to be a market of increased inflammation.
> . . . .
>
> Q. But Mr. Garner doesn't have any of those conditions, does he?
>
> A. What conditions?
>
> Q. Any of the chronic conditions that could cause the markers of this chronic inflammatory process, other than smoking.
>
> A. Right. . . .

(*Id.* at 78:19-79:13, 80:8-14).

Given the absence of evidence supporting his "TRT made the clot bigger" or "TRT interacted with chronic inflammatory disease" theories, both theories are pure speculation, and they are tied to this case only by Dr. Ardehali's *ipse dixit.* They should be excluded.

d. None of Dr. Ardehali's Proposed Biological "Mechanisms" Fits this Case

In his General Report, Dr. Ardehali describes five proposed "mechanisms" by which TRT can cause cardiovascular events. As a preliminary matter, Dr. Ardehali does not identify which "mechanism" out of the five supposedly applies to Garner's case. He also admits that

there is no evidence in Garner's record for four of these five theories. (*See* Ardehali Dep. at 116:3-10, 118:8-15 (thromboxane A2 receptor levels were never measured in Garner); 118:16-119:7, 120:24-121:15 (no evidence of Garner's estradiol levels); 126:4-127:17 (reactive oxygen species ("ROS") is not routinely measured in clinical practice and was never measured in Garner); 130:19-131:1 (activation of endothelial surface receptors ("VCAM") were never measured in Garner)). As for the fifth – increased hematocrit – Dr. Ardehali eliminated this one himself, because Garner's hematocrit was measured after his heart attack, and it was not elevated. (*See id.* at 125:1-22 ("I don't have numbers to suggest that his hematocrit was increased . . . . I would not put too much emphasis on the increase in hematocrit. I don't think it's a significant factor.")). Because there is no evidence tying any of these theories to Garner, Dr. Ardehali should be precluded from discussing his proposed "mechanisms" at trial.

e. All of the Opinions in Dr. Ardehali's General Report Are Inadmissible

i. Dr. Ardehali's General Causation Opinions Do Not Meet *Daubert*'s Standards of Reliability

This Court previously has declined to exclude Dr. Ardehali's general causation opinions. *See* CMO 46, at *9-*14. For the record, Lilly reasserts that Dr. Ardehali's general causation opinions are not based on a reliable methodology and should be excluded. Specifically, Dr. Ardehali:

- Relies on epidemiological studies that fail to demonstrate a statistically significant association between TRT and cardiovascular events for testosterone users as a whole;
- Eschews most of the Bradford Hill factors in favor of an overly speculative "totality of the evidence" methodology;

- "Cherry-picks" studies that support his general causation opinion while criticizing studies with contrary results;
- Relies on irrelevant studies, including animal and in vitro studies and studies involving anabolic steroids;
- Identifies five supposed "mechanisms" by which TRT can allegedly increase the risk of cardiovascular events, though most lack support in literature or in the relevant scientific community. (*See* Ardehali Gen. Report, Ex. 3 to Segura Decl., at pp. 65-80).[2]

While this Court to this point holds a different view, Dr. Ardehali's general causation testimony should be excluded for all of these reasons, as set out previously in AbbVie's Motion to Exclude (Doc. No. 1753), at pp. 10-40, 54-86.

ii. Dr. Ardehali Should Not Be Permitted to Offer Any Opinions about Lilly's Marketing or Promotion of Axiron®

In his General Report, Dr. Ardehali includes several opinions about Lilly's alleged conduct in marketing and promoting Axiron®, including opinions that Lilly marketed and promoted Axiron® for "investigational," "unapproved" and "experimental" uses. (*See* Ardehali Gen. Report at p. 11 ¶ gg, p. 29 ¶ 21, p. 30 ¶¶ 25-26, p. 39 ¶ 4, p. 50 ¶ 50). All of these opinions should be excluded.

First, as a cardiologist, Dr. Ardehali is not qualified to render marketing opinions. In this MDL, plaintiffs previously have agreed that marketing opinions are outside of Dr. Ardehali's expertise. *See In re Testosterone Replacement Therapy Prods. Liab. Litig.*, Case No. 14 C 1748, 2017 WL 1836443, at *19 (N.D. Ill. May 8, 2017) ("CMO 48"); *see also Huskey v. Ethicon, Inc.*,

[2] In particular, there is a lack of reliability regarding testing techniques for the "ROS" theory. (*See* Ardehali Dep. at 126:4-127:17).

29 F. Supp. 3d 691, 722-23 (S.D. W. Va. 2014) (gynecologist had no expertise in marketing and was therefore unqualified to opine on same). There is no reason to change that conclusion here.

Second, Dr. Ardehali admitted during his deposition that he has never seen any Axiron® advertisements or promotional material; indeed, he has never prescribed Axiron® to any of his patients and has only seen Axiron® containers in photographs. (Ardehali Dep. at 39:8-18; *see also id.* at 20:14-17). In fact, Dr. Ardehali could not identify a single Axiron®-specific example of the kind of promotional material he described as being inappropriate in his General Report. (*See id.* at 41:3-14, 42:2-23, 43:20-44:23, 45:11-46:12, 48:7-49:8; *see also id.* at 49:9-50:3, 50:10-22 (admitting that his assertion that Lilly used the Androgen Deficiency in Aging, or "ADAM," screening tool in promoting Axiron® was "a general statement with respect to exogenous testosterone," and not specific to Lilly)). Because Dr. Ardehali has no foundation for any opinions about Lilly's marketing and promotional practices, all of his marketing opinions should be excluded. *See In re Fosamax Prods. Liab. Litig.*, 645 F. Supp. 2d 164, 197 (S.D.N.Y. 2009) (precluding expert from testifying about marketing where he spent less than an hour reviewing defendant's marketing documents, did not read them in detail, and could not recall any of them); *In re Trasylol Prods. Liab. Litig.*, No. 08-MD-01928, 2010 WL 4052141, at *7 (S.D. Fla. May 12, 2010) (excluding anesthesiologist's marketing opinions because "they indisputably lie outside his area of expertise and are not based on any reliable methodology or scientific principle").

iii. Dr. Ardehali Should Not Be Permitted to Offer Any Opinions about Lilly's Supposed Actions or Inaction with Respect to Axiron®

Dr. Ardehali also offers various opinions about Lilly's alleged actions and inaction with respect to Axiron®. For example, he opines that Lilly "failed to adequately investigate the long-

term safety of the administration of testosterone therapy to middle-aged and older men" (Ardehali Gen. Report at p. 9 ¶ s), that Lilly did not adequately test the use of Axiron® in "off-label" populations of patients at increased cardiovascular risk (*id.* at p. 11 ¶ gg; *see also id.* at p. 40 ¶ 8), and that Lilly did not "heed" the supposed "dangers" of testosterone therapy in "Low T" patients (*id.* at p. 29 ¶ 21).

Again, Dr. Ardehali lacks any reliable basis for this testimony as it pertains to Axiron® and Lilly. He testified that his General Report in the Axiron® cases was largely unchanged from what he submitted for other defendants in this MDL (Ardehali Dep. at 15:4-22, 16:20-17:9), and that he did not rely on – or even review – any Lilly company documents in forming his opinions. Dr. Ardehali also did not consider any Axiron® adverse event reports or promotional materials, he did not review the New Drug Application for Axiron® or the depositions of any Lilly employees, and, while he found some clinical studies including Axiron® in a Medline search, he does not know if they were sponsored by Lilly. (*Id.* at 20:5-22:6). As such, none of these opinions rises above the speculative level and they all should be excluded.

2. Dr. Burt Gerstman's Opinions Should Be Excluded

Plaintiffs proffer epidemiologist B. Burt Gerstman, Ph.D. to testify that TRT increases the risk of cardiovascular events. Dr. Gerstman's principal conclusions are:

- "Meta analyses of heart attack and strokes from available clinical trials indicate a 30 to 50 percent increase in risk in [groups treated with testosterone]. Bayesian MCMC analysis demonstrate that the probability of increased risk is at least 80 percent." (Gerstman Report, Ex. 4 to Segura Decl., at p. 10).

- Studies of testosterone supplementation that have used self-controls found approximately a 40% increase in the rate of heart attack following initial prescriptions. This elevated rate returns to baseline following discontinuation of the testosterone supplement. (*Id.* at p. 9).

- There is "substantial and credible epidemiological and biomedical evidence showing that testosterone supplementation increases the risk of heart attack and

> stroke. Based on a synthesis of data and lines of reasoning discussed in this report, testosterone use in older men increases the risk of heart attacks and strokes by approximately 40% on average. This is roughly equivalent to an additional 4 cases of heart attack and stroke per 1000 testosterone users or an additional 9,200 such events based on testosterone utilization estimates for 2013." (*Id.* at p. 132).

a. Dr. Gerstman's Opinions Are Not Reliable

As with Plaintiffs' other general causation experts, this Court has twice declined to exclude Dr. Gerstman's testimony, and Lilly will not rehash in detail why his testimony should be excluded. But Lilly maintains that Dr. Gerstman's opinions should be excluded because they are not the product of reliable methodologies. Specifically, Dr. Gerstman, in place of statistically significant data, substitutes a speculative, subjective, and unreliable post-hoc Bayesian analysis to existing studies that do not utilize this method. Bayesian analysis is not generally accepted in the relevant scientific community, and its application to existing studies has been repudiated by the FDA. In addition, Dr. Gerstman cherry-picks data, selecting and relying on the few studies that support his conclusion, criticizing or simply disregarding the numerous studies that undercut his theories, and drawing unjustified parallels to irrelevant studies of hormone replacement therapy in women. For all of these reasons, Dr. Gerstman's "increased risk" opinions should be rejected.

Beyond these arguments, there are distinct reasons to take a different view of Dr. Gerstman's testimony here. First, Dr. Gerstman confirmed in his deposition that his opinions do not fit Axiron® cases in general and that they particularly fail to fit Garner's very short-term use of Axiron®. He also admitted that studies of TRT do not support his general conclusions. Ultimately, Dr. Gerstman conceded that it is not yet possible to draw a firm conclusion that Axiron® increases the risk of heart attack. Given this testimony, all of Dr. Gerstman's opinions should be excluded for this reason as well.

b. Dr. Gerstman's Opinions Do Not Fit Garner's Case

Because Dr. Gerstman's opinions do not fit the facts of Garner's case – or any Axiron® case – they cannot help the jury resolve any facts in dispute, and they should be excluded. *Daubert*, 509 U.S. at 591 (citing Fed. R. Evid. 702); *see also, e.g.*, *Deimer v. Cincinnati Sub-Zero Prod., Inc.*, 58 F.3d 341, 345 (7th Cir. 1995). Dr. Gerstman admits that he can only "speculate" about the average length of time it takes a TRT patient to reach the therapeutic level of testosterone. (Gerstman Dep., Ex. 5 to Segura Decl., at 119:15-120:1). He does not know how long Axiron® stays in a patient's system after the patient stops using Axiron®. (*Id.* at 120:2-7). He cannot specify the shortest duration of use of testosterone that caused a heart attack or stroke in any study, though he recalls one "just from memory" in which a heart attack occurred within the first two weeks of use. (*Id.* at 149:7-24). He does not know how long it takes testosterone to cause polycythemia. (*Id.* at 153:19-22). And he has no evidence that any of the supposed mechanisms he discusses can cause a heart attack when the duration of use is as short as three days. (*Id.* at 154:7-13).

Through this testimony, Dr. Gerstman effectively concedes that his opinions, like those of Dr. Ardehali, are not broad enough to apply in a case like Garner's where the duration of use was very short. *See In re Hanford Nuclear Reservation Lit.*, 292 F.3d 1124, 1133 (9th Cir. 2002) (appropriate general causation inquiry is whether exposure to the substance "at the level of exposure alleged by plaintiffs[] is capable of causing" the alleged injuries). Moreover, while Dr. Gerstman purports to draw conclusions that sweep in all manufacturers' testosterone products, Dr. Gerstman has done no research about Axiron® beyond reviewing the Axiron® label. (Gerstman Dep. at 25:8-10). He never looked at Axiron® adverse event reports, and never looked specifically at Axiron® clinical trials. (*Id.* at 30:12-20). He does not believe that any

studies on his reliance list involved Axiron®. (*Id.* at 119:1-7). Consequently, Dr. Gerstman's conclusions about Axiron® are nothing more than improper speculation.

c. Dr. Gerstman Admits that There Are No Studies Supporting His "30 to 50 Percent Increase" Conclusion

Exclusion of Dr. Gerstman's testimony is warranted in Lilly's cases for another particularized reason. Dr. Gerstman admits that he reached his "30 to 50" percent increase conclusion by relying on three observational studies he could construe as supporting his theory while ignoring everything else. In his deposition, he was asked how he arrived at his conclusion that testosterone use increases the risk of heart attack and stroke by 30 to 50 percent:

> Q. . . . [Y]ou say, "A consistent thread of elevated risk averaging 30 to 50 percent is seen in observational studies by Finkle, Etminan and Wallis"; correct?
>
> A. Yes.
>
> Q. Those are the only studies that you mention in this paragraph; right?
>
> A. Yes.
>
> Q. Now, I guess my question to you is this notion of consistency. Is it your reading of Finkle, Etminan and Wallis that from those studies, that you get a consistent relative risk of between 30 and 50 percent; is that what you're saying?
>
> A. From those studies, yes.

(Gerstman Dep. at 81:18-82:5). But, when questioned further, Dr. Gerstman admitted that Finkle, Etminan, and Wallis are the only three studies from which this "consistent" relative risk could be found:

> Q. All right. If we looked at all of the studies that you – you reviewed, or at least all the ones that are in your set of reliance materials, putting aside your – your methodological quarrels, I'm just looking at the results, would you say that – that those epidemiological studies that look at the relative risk between testosterone and heart attacks, arrive at a – at a consistent thread of 30 to 50 percent?
>
> A. No.

> Q. Is there a consistent thread that emerges from all the studies that are listed in your reliance materials?
>
> A. Are we restricting the question just to observational studies at this point?
>
> Q. Okay, let's do that. I didn't even think of that, but let's go with it. We're restricting it to observational studies at this point.
>
> A. No.

(*Id.* at 82:6-24). Dr. Gerstman thus admits that he cherry-picked the three observational studies that he could construe as supporting his "increased risk" conclusion and simply left out those that did not. This "selective use of facts fail[s] to satisfy the scientific method and *Daubert*." *Holden Metal & Aluminum Works, Ltd. v. Wismarq Corp*., No. 00 C 0191, 2003 WL 1797844, at *2 (N.D. Ill. Apr. 3, 2003). Exclusion of Dr. Gerstman's testimony is warranted in Lilly's cases for this particularized reason.

d. Dr. Gerstman Admits That Cardiovascular Safety of Testosterone Has Not Yet Been Determined

Finally, yet another particularized ground for exclusion in Lilly's cases emerged from Dr. Gerstman's deposition when he was asked about the conclusion of a 2017 article about testosterone safety. His response is telling:

> Q. No[w], looking at the last sentence of this conclusion, the authors write, "Based on the current evidence, no firm conclusions can be drawn regarding the cardiovascular safety of testosterone therapy." Is that a statement with which you agree or disagree?
>
> A. I agree with that, conditional on it also is recognized that you can't draw any conclusions about dismissing concerns.

(Gerstman Dep. at 127:18-128:2). By specifically admitting that there is not sufficient evidence to conclude that concerns about the cardiovascular safety of testosterone therapy are either warranted or unwarranted, Dr. Gerstman necessarily concedes that his quantified "increased risk" figures – "30 to 50 percent in heart attack and stroke," "40 percent increase in heart attack

following initial prescription" – are nothing more than unvarnished speculation. That does not equate to reliable expert testimony, and Dr. Gerstman's opinions should be excluded based on his admission.

3. Dr. Martin G. Wells Should Be Excluded

Garner proffers Martin G. Wells, Ph.D., who states that he "has been asked to assess the statistical power of extant studies that consider the association between exogenous testosterone therapy and [major adverse cardiac events] ('MACE')." (Wells Report, Ex. 6 to Segura Decl., at p. 1). Dr. Wells's analysis is, however, specifically limited. He is offered only to opine that the Corona and Albert meta-analyses are underpowered and that the Basaria (2010) result is statistically significant.[3] From this premise, he concludes:

> Most of the extant studies . . . have quite limited power to detect a 50% risk. These studies are essentially unable to rule out an increased risk of a MACE due to testosterone therapy and thus fail to prove, or provide assurance about the safety. If one correctly performs a Bayesian inferential meta-analysis methodology using the event count data, there is roughly an 85% probability that testosterone supplementation increases the odds of a MI and stroke. This posterior probability reveals that although a frequentist 95% confidence interval of 0.78-2.72 includes the value one, there is a high probability of a MACE event with testosterone supplementation.

(*Id.* at p. 2).

Dr. Wells's conclusion should be excluded because it is not the result of a reliable methodology and because it cannot aid the jury in resolving the issues in this case. Moreover, under Fed. R. Evid. 403, the opinion should be excluded because its limited probative value is outweighed by the danger that it will confuse and prejudice the jury.

First, Dr. Wells attempts to prove general causation by criticizing the limitations of existing studies to "rule out" a causal connection between testosterone therapy and MACE.

[3] He notes, in his report, that he later reviewed the Alexander study and that it did not change his opinions. (*Id.* at p. 2 n. 3).

Under *Daubert,* backward-looking criticism of epidemiological data is not admissible to show causation. *See, e.g.*, *Norris v. Baxter Healthcare Corp*., 397 F.3d 878, 886 (10th Cir. 2005) (holding that expert could not prove causation by criticizing existing epidemiology); *see also Conde v. Velsicol Chem. Corp*., 24 F.3d 809, 814 (6th Cir. 1994) (explaining that published critiques of studies "underscore the need for further studies" but do not establish causation). The same holds true for Dr. Wells, who employs a subjective post-hoc mode of analysis disfavored by FDA and one that is inadequate to establish causation.

Second, and in any event, Dr. Wells's opinion is inadmissible because it cannot help the jury resolve the issues in Garner's case. Alabama product liability law does not diverge from traditional causation principles: in Alabama, like everywhere else, a plaintiff has the burden of proving general causation. *See Jones v. Novartis Pharm. Corp*., No. 2:13-CV-624-VEH, 2017 WL 553134, at *6 (N.D. Ala. Feb. 10, 2017); *McClain v. Metabolife Int'l, Inc*., 193 F. Supp. 2d 1252, 1258 (N.D. Ala. 2002). Dr. Wells's opinion does not provide affirmative proof of causation. His assertion that general causation cannot be "ruled out" does not help the jury in resolving Plaintiffs' affirmative burden to demonstrate causation. Moreover, because such testimony, uttered by an expert, could potentially confuse the jury on the burden of proof, the potential for prejudice to Lilly is apparent. This supports exclusion as well.

B. No Admissible Expert Testimony Supports Debroka's Blood Clot Claims

Plaintiff Debroka offers general and specific causation opinions from Dr. Henry Rinder, who also opines that the Axiron® label was inadequate. Debroka also offers the specific causation opinion of his treating physician, Dr. Jason Tache. These opinions are inadmissible and each one should be excluded.

1. Dr. Rinder's Opinions Should Be Excluded

a. Dr. Rinder's Specific Causation Conclusion Is Unsupported

As explained in Lilly's Motion for Summary Judgment, Florida law governs the substantive issues in Debroka's case. Under Florida law, Debroka bears the burden of proving, through competent specific causation testimony, that Axiron® was more likely than not a substantial factor in causing his DVT. *See Haller v. AstraZeneca Pharms. LP*, 598 F Supp. 2d 1271, 1304 (M.D. Fla. 2009) (court must determine whether defendant's conduct was a "material and substantial factor in bringing [the injury] about"); *Guinn*, 602 F.3d at 1256 (citing *Gooding v. Univ. Hosp. Bldg., Inc.*, 445 So.2d 1015, 1018 (Fla. 1984)); *Bradley v. Lorillard Tobacco Co.*, No. 8:13-cv-227-T-33AEP, 2014 WL 5780428, at *3 (M.D. Fla. Nov. 5, 2014).

Here, Dr. Rinder's specific causation opinion does not meet this "substantial factor" causation burden for the same reasons that this Court excluded the plaintiff's specific causation expert, Dr. Abbas, in the Auxilium litigation. There, Dr. Abbas' opinion that TRT caused plaintiff Owens' DVT was "based on the premise that Owens applied Testim as prescribed and used the full, therapeutic dose." CMO 76, at *7. Dr. Abbas had no opinion on whether Testim could cause DVT if misapplied or if the user applied less than the full dose; yet the evidence of record in plaintiff Owens's case showed that he did not apply Testim as instructed, and did not use the full dose. *Id.* Accordingly, the Court concluded that Dr. Abbas' opinion did not fit the facts of the case and was therefore irrelevant and inadmissible. *Id.*

Similarly, Dr. Rinder's specific causation opinion rests on assumptions that are not supported or supportable. He relies on a study by Martinez et al. which, according to Dr. Rinder, found an increased DVT risk in "current users" of TRT, and classified individuals as "current users" for an additional 30 days after they ceased using TRT. (Rinder Dep., Ex. 8 to Segura Decl., at 406:1-23). Dr. Rinder's conclusion that TRT caused Debroka's DVT rests on the

assumption that Debroka stopped using Axiron® less than 30 days before he developed his DVT. (*See* Rinder Debroka Report, Ex. 9 to Segura Decl., at p. 3; Rinder Dep. at 351:12-352:14, 388:13-389:15). But, as with Mr. Owens, the evidence does not support this assumption.

In particular, it is unclear from the record exactly when Debroka received and used his 30-day Axiron® sample. Debroka testified that he began using Axiron® the second week of November 2013, although he was unsure of the exact dates. (Debroka Dep., Ex. 2 to Declaration of Kevin J. Lohman in support of Debroka Motion for Summary Judgment ("Lohman Decl."), at 41:12-22). But Debroka saw his prescriber on October 25, not in November. (*See* Rinder Dep. at 379:13-380:17). In addition, much like Mr. Owens, Debroka testified that he used Axiron® inconsistently and that, contrary to the label instructions, he occasionally applied multiple pumps of Axiron® in a single day (Debroka Dep. at 202:19-203:13, 204:7-205:18), both of which would have affected the date on which he finished his sample even if he did not begin using it until mid-November. With no clear record of when Debroka started and stopped using Axiron®, Dr. Rinder cannot support the assumption that Debroka was a "current user" as defined by the Martinez study. His opinion, therefore, does not fit the facts of Debroka's case, and, just as with Mr. Owens, should be excluded.

b. Dr. Rinder Should Not Be Permitted to Introduce His "Estradiol" and "Platelet Aggregation" Theories

Dr. Rinder proposes a number of "mechanisms" in his general report by which TRT can supposedly cause VTE. For two of these supposed "mechanisms" – elevated estradiol levels and platelet aggregation – Dr. Rinder admits that confirmatory testing was not performed at the time of Debroka's DVT, thereby leaving the record devoid of evidence that either mechanism was possible. (*See* Rinder Dep. at 354:9-20 (estradiol levels not tested); 354:22-355:8 (platelet

aggregation not tested)). Since these supposed mechanisms are not relevant to Debroka's case, Dr. Rinder should not be permitted to testify about either one.

c. Dr. Rinder's General Causation Opinion Does Not Meet *Daubert*'s Standards of Reliability

This Court previously has declined to exclude Dr. Rinder's general causation opinion. *See* CMO 46, at *14-*16. Nevertheless, Lilly maintains that Dr. Rinder's general causation opinion is not the product of a reliable methodology. In reaching this opinion, Dr. Rinder utilized an impermissibly speculative "totality of the evidence" methodology, and he failed to identify a statistically significant association between TRT and VTE in epidemiological literature. He also cites irrelevant animal studies and female hormone studies, and relies to excess on anecdotal case reports and adverse event reports to support his general causation opinion. For all of these reasons, as has previously been argued by AbbVie (Doc. No. 1753), at pp. 40-47, 86-100, Dr. Rinder's general causation opinion should be excluded.

d. Dr. Rinder Is Not Qualified to Opine on the Adequacy of the Axiron® Label

Dr. Rinder is a medical doctor specializing in hematology. His General Report focuses on the mechanisms by which he believes TRT can cause VTE and does not set forth opinions about the adequacy of the Axiron® label. (*See generally* Rinder Gen. Report, Ex. 10 to Segura Decl.). During his deposition, however, Dr. Rinder suggested that the Axiron® VTE warning was "vague":

> Q. … If you look with me on the fourth line [of the 2010 label], it says, "An increase in red blood cell mass may increase the risk of thromboembolic events." Did I read that correctly?
>
> A. You did.
>
> Q. Okay. So from the time Axiron® was approved for use on the U.S. Market, FDA was aware, and always knew, so it made sure that it was included in the label, that there was the potential for an increase in hematocrit and that an

> increase in the red blood cell mass may indeed increase the risk of thromboembolic events, meaning DVT or PE; is that correct?
>
> A. So, yes, this has – this has been there since the 2010. When I read this as a clinical person, it's a little bit vague. If hematocrit becomes elevated, there's no real guideline to what that is. And so it's a little bit hard to understand but in a general way it's mentioned there. Yes.

(Rinder Dep. at 112:7-113:10 (objection omitted); *see also id.* at 114:21-24 ("As to other physicians who may not know the data regarding red cell mass and thromboembolic events, this is very vague.")). Dr. Rinder specified that his problem with the label was that "what constitutes an increase that may require lowering or discontinuation, that's just not there." (*Id*. at 117:15-19).

Dr. Rinder is not qualified to opine on the adequacy of the Axiron® label. He has not "done any work on what are the specific components of what must be in a label and what are the regulatory requirements related to that." (*Id.* at 21:23-22:3). Ultimately, he was forced to concede that he wasn't a labeling expert:

> Q. You are not holding yourself out as a labeling expert or as to whether the Axiron® label was adequate and provided adequate warnings, true?
>
> A. Not as an expert in that respect, no.

(*Id*. at 22:8-13*; see also id*. at 23:6-10 ("I'm not holding myself out as to understanding the regulatory components of what [FDA] deem adequate, what they deem inadequate. I can't speak to that.")). Accordingly, this Court should preclude Dr. Rinder from offering any opinions about the adequacy of the Axiron® label. *See* CMO 46, at *6 (expert must be qualified on specific topic, not just in general, to satisfy *Daubert*).

2. Dr. Tache's Proposed Opinions Are Inadmissible in the Absence of an Expert Report

Debroka has disclosed the "anticipated" specific causation testimony of one of his treating physicians, Dr. Tache. He is a physician who treated Debroka when he was hospitalized

with his DVT. The Rule 20(a)(2)(C) disclosure filed by Debroka states that Dr. Tache is expected to testify that Axiron® was a "substantial factor" in causing Debroka's DVT. In this case, this opinion exceeds the bounds of permissible testimony for a non-retained expert and it should be excluded from trial.

An expert witness retained or specially employed in order to give expert testimony in a case must submit a written expert report. Fed. R. Civ. P. 26(a)(2)(B). A non-retained expert, such as a treating physician, can testify without submitting a written report, but only to opinions formed during the course of his or her treatment of the plaintiff. *E.E.O.C. v. AutoZone, Inc*., 707 F.3d 824, 833 (7th Cir. 2013) (citing *Meyers v. Nat'l R.R. Passenger Corp*., 619 F.3d 729, 734-35 (7th Cir. 2010)). Causation opinions that are "too far afield from treatment choices" are not admissible in the absence of an expert report. *See In re Zimmer Nexgen Knee Implant Prods. Liab. Litig.*, No. 12 C 6279, 2015 WL 3799534, at *8 (N.D. Ill. June 17, 2015); *see also Brunswick v. Menard, Inc*., No. 2:11 CV 247, 2013 WL 5291965, at *4 (N.D. Ind. Sept. 19, 2013) ("If a treating physician intends to testify beyond his observations, he must provide a full expert report.").

Here, the "summary disclosure" of Dr. Tache's anticipated testimony contains several categories of opinions that are "too far afield" from Dr. Tache's treatment. As a preliminary matter, Dr. Tache plans to offer testimony about:

- The methodology of diagnosing DVTs;
- The treatment of DVTs;
- The diagnosis and treatment of provoked versus unprovoked DVTs;
- The determination of whether a DVT is acute or chronic;
- The risk factors that cause DVTs; and

- The determination of the cause or causes of a DVT.

(Tache Disclosure, Ex. 11 to Segura Decl., at pp. 1-2). Dr. Tache may not opine on any of these topics because he did not submit an expert report. *See, e.g.*, *In re Zimmer*, 2015 WL 3799534, at *5 (noting that physician's opinions regarding the "forces in the knee, edge loading, implant lift-off, and the adequacy of Zimmer's testing" would be excluded because they "exceed the scope of [physician's] treatment and [were not] presented in an expert report identifying the facts and data supporting his conclusions").

Dr. Tache's disclosure also includes the opinion that "Mr. Debroka's use of Axiron® was a substantial factor in causing his DVT." (Tache Disclosure at p. 3). There is no indication that Dr. Tache formed this opinion when he was treating Debroka. Indeed, the sole medical record dictated by Dr. Tache during Debroka's hospitalization does not mention Axiron® at all, stating only (incorrectly) that "[t]he patient's only identifiable risk factor is testosterone use." (DEBROKAJ-10PPR-00063-65, Ex. 10 to Lohman Decl.). The record also indicates that Dr. Tache subsequently ordered a hypercoagulable workup, which revealed that Debroka had two additional risk factors for DVT: weak lupus anticoagulant and single R506Q mutation (heterozygote) Factor V Leiden. This opinion thus must be excluded as well. As a non-retained expert who has not submitted a report, Dr. Tache's permissible testimony is limited to observations he made and conclusions he reached during the course of his very brief treatment of Debroka. While he can testify that he listed TRT as a "risk factor" for Debroka's DVT, he may not go beyond his records to opine that Axiron® was a "substantial factor in causing" Debroka's DVT. *See Zitska v. Village of Westmont*, No. 07 C 0949, 2011 WL 4738249, at *11-*12 (N.D. Ill. Oct. 7, 2011) (granting defendants' motion to bar plaintiff's treating physicians from offering causation opinions).

C. Dr. Peggy Pence's Opinions Should Be Excluded

Peggy Pence, Ph.D., states that her "assignment" was to "address and analyze" Lilly's "actions" regarding Axiron® with respect to drug approval, product labeling, marketing and promotional activities, and postmarket surveillance. (Pence Report, Ex. 12 to Segura Decl., at p. 6). Throughout her 90-page expert report, in the guise of expert opinions, she regurgitates the content of Lilly's corporate documents, speculates about Lilly's "knowledge" and "intent" and further about why the FDA acted and failed to act. This speculative dissertation is followed by Dr. Pence's own series of legal and regulatory conclusions. None of this is proper expert testimony, and it should be excluded.

1. Dr. Pence's Narrative Regurgitation of Lilly's Corporate Documents Improperly Invades the Province of the Jury

Nearly forty pages of Dr. Pence's report are devoted to her own narrative spin applied to dozens of Lilly company documents. (*See generally* Pence Report). This purported narrative may be appropriate for Plaintiffs' closing arguments, but, as courts across the country have widely held, it is neither appropriate nor admissible in the guise of expert testimony. *See, e.g.*, *In re C.R. Bard, Inc*., 948 F. Supp. 2d 589, 608 (S.D. W. Va. 2013), on reconsideration in part (June 14, 2013) (expert testimony inadmissible when it "merely regurgitates factual information that is better presented directly to the jury rather than through the testimony of an expert witness") (quoting *Hines v. Wyeth*, No. 2:04–0690, 2011 WL 2680842, at *5 (S.D. W. Va. July 8, 2011)); *see also In re Fosamax Prods. Liab. Litig*., 645 F. Supp. 2d at 192 ("An expert cannot be presented to the jury solely for the purpose of constructing a factual narrative based on the record of evidence.").

But the jury can review Plaintiffs' admissible documentary evidence for itself and can draw its own inferences. Given that, Dr. Pence should be precluded from invading the province of the jury with her inadmissible advocacy.

2. Dr. Pence's Opinions Are Inadmissible Legal Conclusions

Dr. Pence further opines that "[t]he Axiron® Defendants improperly marketed and promoted Axiron® for off-label uses, including late-onset hypogonadism . . . . Thus, the Axiron® Defendants marketed and sold a misbranded product, in violation of federal regulations and the industry standard of care." (Pence Report at p. 91 (Opinion 3)). These statements represent conclusions of law, applying Dr. Pence's interpretations of federal regulations to her "spin of documentary evidence." This Court, again in accord with courts across the country, has acknowledged that such conclusions are improper expert testimony and are inadmissible. *See, e.g.*, *Good Shepherd Manor Found., Inc. v. City of Momence,* 323 F.3d 557, 564 (7th Cir. 2003) ("[E]xpert testimony as to legal conclusions that will determine the outcome of the case is inadmissible."); *Client Funding Solutions Corp. v. Crim,* 943 F. Supp. 2d 849, 863 (N.D. Ill. 2013) ("Opinions that amount to legal conclusions do not assist the trier of fact. . . ."). Dr. Pence's proposed testimony about Lilly's alleged "off-label" marketing, violations of federal regulations, and "misbranding" of Axiron® should be excluded as well.

3. Dr. Pence's Speculation Regarding FDA's Reasons for Acting or Not Acting, As Before, Should Be Excluded

As she has in cases against other manufacturers, Dr. Pence also testified that FDA's post-marketing activities with respect to Axiron® were limited by its supposed lack of resources:

> Q. With respect to post-marketing activities for Axiron®, so after November of 2010, do you have an opinion that the FDA was in any way burdened by a lack of resources in terms of all the post-marketing monitoring of Axiron®, including adverse events?

> A. Well, certainly, the reports we were just discussing show that there were lack -- there was a lack of resource in various data, issues with regard to FDA being able to follow up on all track safety issues, and that sort of thing.

(Pence Dep., Ex. 13 to Segura Decl., at 156:18-157:2).

Similarly, after criticizing certain advertising materials related to Axiron®, Dr. Pence was asked whether FDA took action with respect to those advertisements. She answered, ". . . [W]e talked about IOM and GAO reports where it was evaluated and in – where OPDP or DDMAC, then OPDP, their ability to evaluate ads was assessed and it was noted that DDMAC, then OPDP, has very limited resources and only reviews a very small portion of the ads that it actually gets." (*Id.* at 228:23-229:9).

This Court has twice excluded similar testimony, and it should do so again. In CMO 48, ruling on AbbVie's motions, this Court held, "Dr. Pence lacks a sufficient basis to testify regarding why the FDA acted (or failed to act) and . . . this particular opinion would be inadmissible in any event, either as speculative, unhelpful to the jury, or unfairly prejudicial under Rule 403." CMO 48, at *16. More recently, in CMO 76, ruling on Auxilium's motions, this Court confirmed that Pence "is prohibited from speculating about why the FDA acted or failed to act." CMO 76, at *9. These rulings apply with equal force in Lilly's cases.

4. Dr. Pence's Improper "State of Mind" Opinions Are Inadmissible

In CMO 48, this Court acknowledged the well-settled law holding that an expert may not permissibly testify about a party's "state of mind" or "intent." CMO 48, at *13; *see also, e.g.*, *Baldonado v. Wyeth*, No. 04 C 4312, 2012 WL 1802066, at *8 (N.D. Ill. May 17, 2012) (precluding expert from offering opinion testimony as to defendant's state of mind, including intent or motivation). Dr. Pence runs afoul of this principle by using her improper narrative about Lilly's company documents as the basis of speculation about what Lilly "intended."

For example, she opines, "From the time of premarketing product development and pre-launch, the Axiron® Defendants' 'intended use' of Axiron® included indications that were not in the approved and class labeling for the product." (Pence Report at p. 91 (Opinion #1)). Dr. Pence also opines repeatedly about what Lilly supposedly "knew." For example, she states that:

> The Axiron® Defendants knew and understood that Axiron® was being prescribed off-label to patients, including those with late-onset hypogonadism (low testosterone due to aging and chronic illnesses). . . . The Axiron® Defendants knew or should have known of serious concern regarding a potential increase of cardiovascular events with testosterone use in high-risk populations.

(*Id.* (Opinion #4)). And among numerous other examples, Dr. Pence also opines that the "Axiron® Defendants marketed to and were aware that Axiron® was being used in an off-label population of men for whom there was no substantial evidence of either safety or clinical efficacy" (*id.* at p. 57, ¶ 220), and the "Axiron® Defendants knew Axiron® was not approved to treat age-related or late-onset hypogonadism." (*Id.* at p. 58, ¶ 226).[4]

In CMO 76, this Court declined to preclude Dr. Pence from offering testimony about "intended use" in the Auxilium cases because the testimony would provide a "framework by which the jury can assess what Auxilium intended via its marketing." At the same time, it cautioned that, while Dr. Pence could "walk up to the line," she could not cross it and "offer a conclusion about what Auxilium intended." CMO 76 at *22 (internal punctuation and citation omitted). If the Court permits Dr. Pence to testify in Lilly's cases, it should similarly limit her "intent" conclusions.

[4] In her report, Pence cites documents that purportedly demonstrate that "correspondence from the FDA" had confirmed to Lilly that Axiron was not approved to treat age-related or late-onset hypogonadism. (Pence Report at p. 41 n. 161). But, shown these documents at her deposition, Pence admitted that they were not official FDA documents and were not directed to Lilly, and that she has no evidence that Lilly knew of these materials before Plaintiffs used Axiron. (Pence Dep. at 191:10-210:11).

D. David J. Handelsman's Opinions Should Be Excluded

Plaintiffs have produced the report of David J. Handelsman, MB BS, FRACP, Ph.D., FAHMS, an endocrinologist and medical school professor who lives in Australia. Although Dr. Handelsman's report includes testimony to the effect that testosterone increases the risk of certain adverse events, Plaintiffs previously have represented that they do not intend to elicit "causation" testimony from Dr. Handelsman. Instead, they expect Dr. Handelsman to testify about Lilly's marketing of Axiron®, including supposed off-label marketing, and the effects of Lilly's marketing practices on prescribing physicians. These opinions are inadmissible under Rules 702 and 403.

1. Dr. Handelsman's Opinions Should Be Excluded on the Same Grounds as Before

In CMO 48, this Court held that Dr. Handelsman was not qualified "to opine about whether the evidence indicates that AbbVie was engaged in 'disease mongering' . . ." CMO 48, at *18. The Court also held that Dr. Handelsman was precluded from using "pejorative adjectives" (*id.*), and was precluded from offering opinion that was "basically a value judgment regarding AbbVie's conduct . . . ." *Id.* at *19. Finally, this Court held that "the cause-and-effect relationship between AbbVie's marketing campaigns . . . and overprescribing" were "outside [Dr. Handelsman's] area of expertise." *Id.* at *18. Dr. Handelsman offers similar opinions in his report in these cases, and the Court should exclude them here, too.

Specifically, opinions numbers 19, 20, and 25 in Dr. Handelsman's "Summary of Opinions," discussing "disease mongering," as well as the text in his Report amplifying these opinions, should be excluded. In addition, Dr. Handelsman should be precluded from using the adjectives "opportunistic" and "irresponsible" in connection with opinion number 17. Finally, Dr. Handelsman should be precluded from offering opinions 25, 26, 27, 28 and 30 to the extent

that they relate to an alleged cause-and-effect relationship between Lilly's marketing practices and overprescribing or off-label prescribing of Axiron®.

2. Dr. Handelsman's Generic Opinions Do Not Fit the Facts of These Axiron® Cases

There are, however, additional reasons to exclude Dr. Handelsman's opinions in Lilly's cases, principally because he does not connect these opinions to the facts of Lilly's cases. The lynchpin of Dr. Handelsman's marketing testimony is that the so-called "invention" of a condition called "Low T" or "andropause" was the basis of marketing campaigns that resulted in "overprescribing" of testosterone for this "imaginary" condition. (*See generally* Handelsman Report, Ex. 14 to Segura Decl., at pp. 51-60, 66-72). Dr. Handelsman makes only one cursory attempt to tie this theory to Lilly, stating:

> More specific studies examining the effects of testosterone on the co-morbidities associated with ageing such as obesity, diabetes and metabolic syndrome are still warranted. . . . However, the status of off-label testosterone use was well known to and fueled by the pharmaceutical industry amongst others, including the sellers and marketers of Axiron®, resulting in excessive and unjustified testosterone prescribing driven by disease mongering and pharmaceutical industry opportunism.

(*Id.* at p. 75).

But in his deposition, Dr. Handelsman admitted that he had no basis for relating any of these allegations to Lilly or to Axiron®. He admitted that there was no evidence that Lilly was involved in unbranded marketing for testosterone. (Handelsman Dep., Ex. 15 to Segura Decl., at 40:9-22). He had done little or no Axiron®-specific review or analysis related to his marketing opinions or any other opinions in his report. And he had no evidence that his opinions properly applied to Lilly:

- Asked if he ever spoke with any U.S.-based physicians about the impact of Axiron® marketing on them, Dr. Handelsman answered, "No, I did not." (*Id.* at 54:1-7).
- Dr. Handelsman admitted that references in his report to the ADAM questionnaire were left over from his AbbVie report, and that he was not aware of any evidence that Lilly ever used the ADAM questionnaire. (*Id.* at 54:8-23).
- He admitted that he was not aware if FDA ever indicated that Lilly's marketing materials ever failed to comply with federal standards or regulations. (*Id.* at 54:24-55:2).
- He never saw any correspondence from the FDA to Lilly suggesting that marketing materials for Axiron® were inappropriate in any way. (*Id.* at 55:3-9).
- He never considered any Adverse Event reports related to Axiron®. (*Id.* at 56:15-18).
- He never reviewed any Axiron® NDA or any clinical studies Lilly submitted to the FDA before Axiron® was approved, and had only minimal familiarity with studies conducted after Axiron® was approved. (*Id.* at 56:19-57:20).
- He could not identify specific Lilly-generated promotional materials or advertising materials for Axiron® that used the phrase "low-T." (*Id.* at 63:11-18).
- He never reviewed the testimony of sales representatives who visited Garner's or Debroka's prescribing physicians. (*Id.* at 63:19-23).
- He has never seen any evidence that Lilly sales representatives ever used the phrase "low T" to physicians. (*Id.* at 63:24-64:2).

Ultimately, Dr. Handelsman was forced to concede that he did not know for a fact that Lilly ever used the phrase "low-T" in connection with Axiron®, either in its written marketing materials or in communications with physicians. (*Id.* at 64:3-8). And, despite the few token references in his report, he did not review, and could not describe, any evidence suggesting that his "overpromotion for low-T" theory has any relevance to any claims related to Axiron®.

As *Daubert* makes clear, Rule 702 requires that expert testimony be "sufficiently tied to the facts of the case that it will aid the jury in resolving a factual dispute. The consideration has been aptly described . . . as one of 'fit.'" *Daubert*, 509 U.S. at 591; *see also, e.g.*, *Deimer*, 58 F.3d at 345 (affirming exclusion of expert, holding that "testimony must 'fit' the issue to which the expert is testifying to the extent that it is tied to the facts of the case and will aid the jury in resolving a factual dispute"). Dr. Handelsman admits that he cannot tie his "overpromotion" marketing opinions to Lilly or to Axiron®. He did not even try to. Therefore, his opinions do not "fit" the facts of these cases, cannot possibly aid the jury in resolving any issue in these cases, and are inadmissible under *Daubert* and Fed. R. Evid. 702.

3. Dr. Handelsman's Opinions Should Be Excluded Because He Admits He Cannot Tie Them to Plaintiffs or Their Physicians

Dr. Handelsman's report offers a one-sentence conclusion about Debroka: "Based upon the reported testosterone level and clinical history that I have been provided with, there is no evidence that this patient has classical hypogonadism." (Handelsman Report at p. 76). He offers the exact same conclusion – and only that conclusion – about Garner. (*Id.* at 79). For both Plaintiffs, however, Dr. Handelsman admitted that he never reviewed any medical records (or even asked for them), never reviewed any physicians' depositions, and never examined Plaintiffs, took their medical histories, or even spoke to them. He does not know when either

Plaintiff started using Axiron®, when he stopped, how long he used Axiron®, whether he was given instructions for using the product or whether he used it according to the label directions.

There is more. Dr. Handelsman admits that he doesn't know what motivated either Plaintiff to use TRT, or whether either Plaintiff, or either Plaintiff's physicians, ever saw any Axiron® advertisements or television commercials or any Lilly promotional materials. He likewise doesn't know whether either physician reviewed or relied on guidelines from the Endocrine Society or from any other medical society or if those physicians ever saw Lilly's sales representatives, relied on information provided by sales representatives, or relied on information that came directly from Lilly. Finally, he does not know when either physician began prescribing TRT, what motivated either to begin using Axiron®, or what type of risk-benefit analysis either physician used to decide that a patient was appropriate for testosterone therapy. (Handelsman Dep. at 225:10-228:3, 239:17-242:11). Given these admissions, Dr. Handelsman plainly has no foundation for any opinions specific to Lilly's cases.

Yet, undeterred by his avowed lack of knowledge, Dr. Handelsman had no trouble speculating at his deposition about Garner's prescribing physician:

> Since I don't know the basis of [his decision], it's hard to disagree with it, but I do find it very hard to accept and I don't agree – I don't agree that treatment with testosterone under these conditions with this information is satisfactory. I believe that it's the sort of thing that the mass media, advertising, unbranded through patients, branded to the physicians, plus or minus other kind of information, in general terms, persuades doctors when they have a difficult problem and they're told someone has fatigue, fatigue, they think of testosterone, measure it, put him on testosterone. That whole process I think was the drive that's been going on. So that I think is mistaken, I think it's unwise, and I think it's part of the low-T phenomenon and a use of testosterone where it isn't justified.

(Handelsman Dep. at 228:4-23).

Given what he does not know, it comes as no surprise that Dr. Handelsman ultimately was forced to concede that he cannot tie any of his theories to Plaintiffs or their treaters:

> Q. Sitting here today, you can't say with any reasonable medical or scientific certainty that either Mr. Garner's or Mr. Debroka's physicians were influenced by direct-to-consumer advertisements, can you? You just don't know, do you?
>
> A. Not on an individual-doctor level, no.
>
> Q. Okay. Same thing: You can't state with any reasonable degree of medical or scientific certainty whether Mr. Garner's or Mr. Debroka's physicians were influenced by any medical or association guidelines.
>
> A. No, I wouldn't know that. But we know that there were influenced generally by direct-to-consumer advertising in the unbranded, in the unbranded form.
>
> Q. How do you know that either one of these prescribing doctors were influenced by any unbranded advertisement?
>
> A. Not specifically individually, but as a group, yes.
>
> Q. Okay. But you can't say for either one of them that they were influenced by unbranded marketing or branded marketing or clinical practice guidelines. You just don't know, do you?
>
> A. I do not know. That's correct.

(*Id.* at 242:24-243:21).

Daubert requires that admissible expert testimony be "sufficiently tied to the facts of the case that it will aid the jury in resolving a factual dispute." *Daubert*, 509 U.S. at 591 (citing Fed. R. Evid. 702); *see also, e.g.*, *Deimer*, 58 F.3d at 345. Here, Dr. Handelsman admits that his theories cannot be "sufficiently tied to the facts" of Debroka's or Garner's case. As such, Dr. Handelsman's opinions do not fit the facts of these cases, cannot possibly aid the jury in resolving any factual dispute, and should be excluded in their entirety.

IV. CONCLUSION

For reasons unique to its bellwether cases, Lilly respectfully requests that this Court limit the testimony of Plaintiffs' experts as set forth above.

Dated: November 21, 2017

By: */s/ David E. Stanley*

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CERTIFICATE OF SERVICE

I, David E. Stanley, certify that on November 21, 2017, I served a true and correct copy of the foregoing *DEFENDANTS ELI LILLY AND COMPANY AND LILLY USA, LLC'S MOTION AND MEMORANDUM OF LAW IN SUPPORT OF MOTION TO EXCLUDE EXPERT TESTIMONY* on all counsel of record by electronic notice through the CM/ECF system of the United States District Court for the Northern District of Illinois.

/s/ David E. Stanley
David E. Stanley